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Depressive symptoms are prominent among elderly hospitalised heart failure patients

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Abstract

Background: There are limited data on the prevalence of depressive symptoms in hospitalised elderly HF patients and demographic and clinical characteristics associated with depressive symptoms are not known.
Methods: A sample of 572 HF patients (61% male; age 71±12 years; LVEF 34%±15) was recruited from 17 Dutch hospitals during HF admission. Depressive symptoms were assessed by the CES-D. Demographic, clinical variables and HF symptoms were collected from patient chart and interview.
Results: Forty one percent of the patients had symptoms of depression with women significantly more often reporting depressive symptoms than men 48% vs. 36% ($\chi^2=8.1$, $p<0.005$). HF patients with depressive symptoms reported more clinical HF symptoms than patients without depressive symptoms. Even after deleting HF related symptoms (sleep disturbances and loss of appetite) from the CES-D scale, 36% of patients were still found to have symptoms of depression. Multivariable logistic regression analyses revealed that depressive symptoms were associated with female gender (odds 1.68, 95% CI 1.14–2.48), COPD (odds 2.11, 95% CI 1.35–3.30), sleep disturbance (odds 3.45, 95% CI 2.03–5.85) and loss of appetite (odds 2.61, 95% CI 1.58–4.33).
Conclusions: Depressive symptoms are prominent in elderly hospitalised HF patients especially in women. Depressive symptoms are associated with more pronounced symptomatology, despite the fact that other indices of severity of left ventricular dysfunction are similar.

Keywords: Heart failure; Depressive symptoms; Elderly patients; Symptoms of heart failure

1. Introduction

Despite advances in medical treatment, the prognosis of heart failure (HF) remains poor [1]. HF is a chronic disease, which may confront patients with numerous threats including impaired physical functioning and changes in future perspectives. Response to this can be emotional disbalance and depression. Studies that have reported on the prevalence of depression in HF patients mostly evaluate the risk on morbidity and mortality [2–5]; however, only a few studies have investigated the relation between patient or clinical characteristics and depressive symptoms. The few studies that have investigated the demographic and clinical factors related to depressive symptoms have used various diagnostic tools for assessing depressive symptoms. The Beck Depression Inventory scale (BDI) is most often used in these studies. The BDI is known to focus substantially on somatic items and therefore may be inadequate as an instrument to screen for depressive symptoms in HF patients [2]. In some studies, the Center for Epidemiological Depression Scale (CES-D) is used. It has only two somatic items that are similar to the somatic symptoms in HF patients and is therefore a reliable and well-validated

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questionnaire to screen for depressive symptoms in HF patients. [3–7]. The studies describing depressive symptoms in HF have used relatively small sample sizes and rather young patient samples: the mean age in most studies was below 65 years of age. Focusing on these 'relatively young' patients may not be representative for the present 'real life' HF population. Finally most of the studies about HF and depression or depressive symptoms were performed in the United States [4,5,8–14]; only a few have been performed in Europe [15–17].

It is hard to diagnose depression in diseases in which symptoms of the disease are similar to symptoms of depression [18]. In HF patients, symptoms like fatigue, sleeplessness, loss of appetite, feelings of worthlessness and low energy are common. The same symptoms are used to diagnose depression [19]. This is why it is difficult to distinguish depressive symptoms from worsening HF.

To carefully look at symptoms of depression in HF patients we assessed the occurrence of depressive symptoms in hospitalised, elderly HF patients and explored related demographic and clinical factors.

More specifically the following research questions are addressed:

- What is the prevalence of depressive symptoms in elderly hospitalised HF patients?
- Which demographic and clinical variables are related to depressive symptoms in elderly hospitalised HF patients?
- What is the relationship between depressive symptoms and symptoms of HF?

2. Methods

2.1. Participants

Patients in the present study were included in a multi centre HF trial (Coordinating study evaluating Outcomes of Advising and Counselling in HF patients—COACH) conducted in the Netherlands [20]. Data on depressive symptoms that are reported in this study were collected from baseline interviews, before any intervention took place. The study design has been described elsewhere [20]. A summary of the inclusion and exclusion criteria used, is as follows. All patients were admitted for HF (NYHA II–IV). Patients were at least 18 years of age, with evidence of structural underlying heart disease. Patients were excluded if they were enrolled in a study requiring additional visits to research health care personnel. Other reasons for exclusion were invasive intervention within the last 6 months (PTCA, CABG, HTX, valve replacement) or planned during the following 3 months; being in the end stage of another life threatening disease or having a psychiatric diagnosis. In total, 572 patients (of the included 737 patients) having complete data sets of CES-D and HF symptoms were included in the analysis. The Central Ethics Committee approved the study and prior to the announcement of the investigation all patients provided written informed consent. The investigation conforms with the principles outlined in the Declaration of Helsinki.

2.2. Study measurements

2.2.1. Depressive symptoms

The definition of depressive symptoms used in this study is taken from the fourth edition of the Diagnostic and Statistical Manual of Mental Disorder-Fourth Edition (DSM-IV) [14,19]. Depression due to a general medical condition (e.g. heart failure), is defined as: patient's clinical presentation which is dominated by a mood disorder that persists and is characterized by either or both depressed mood or markedly decreased interest or pleasure in nearly all activities, or mood that is elevated, expansive or irritable [14,19].

The Center for Epidemiological Studies Depression Scale (CES-D) was used to assess depressive symptoms of the patients under investigation. The CES-D is a 20-item self-report questionnaire designed to measure depressive symptomatology in the general population and in the medically ill [6,7]. The scale is purported to measure the presence of depressive mood by asking respondents to rate how often they have experienced each of the 20 symptoms during the past week. Each item is scored on a four-point scale: (0) 'rarely or non of the time' (less than once a week), (1) 'some or a little of the time' (1–2 days of the week), (2) 'occasionally or a moderate amount of time' (3–4 days a week), or (3) 'most or all of the time' (5–7 days a week). The total score for a respondent consists of a sum score to the responses to all 20 items, ranging from 0 to 60, with higher scores indicating more symptoms of depression (weighted by the occurrence during the past week.) A cut-off point of 16 is generally used to define patients who are at risk for clinical depression [3,21]. The CES-D is a valid instrument to identify high-risk groups and to study the relationships between depressive symptoms and many other variables, which has been established in cardiac and non-cardiac patients [23,24,26].

2.2.2. Demographic and clinical data

During admission to the hospital, data on demographics: age, sex, living situation and educational level were collected from patient interview. Left ventricular ejection fraction (LVEF), NYHA functional class at admission, aetiology, duration of HF and the presence of co-morbidities (hypertension, COPD, Type II diabetes mellitus, peripheral vascular disease, renal dysfunction, arthritis and cerebro-vascular accident) was collected from medical records.

2.2.3. Symptoms of HF

Symptoms of HF were assessed from an interview comprising ten structured questions. During this interview,

Table 1
Patient characteristics and univariate differences between patients with and without depressive symptoms

	Total group	No depressive symptoms	Depressive symptoms	*P* value
	n = 572	*n* = 339	*n* = 233	
	Mean ± sd	Mean ± sd	Mean ± sd	
Demographics				
Age	71 ± 12	71 ± 12	70 ± 12	0.16
Sex (female)	38%	52%	48%	0.004*
Living with a partner	61%	62%	57%	0.24
Education level				
At least six years of primary school	55%	55%	55%	0.77
Diploma secondary school	30%	28%	32%	
Higher education or university	15%	16%	13%	
Clinical characteristics				
LVEF (%)	34 ± 15	33 ± 14	34 ± 15	0.52
LVEF <40%	32%	71%	63%	0.07
NYHA II, III, IV (at admission %)	6, 51, 43	6, 50, 44	6, 52, 42	0.60
Serum creatinine (mmol/L)	122 ± 45	120 ± 41	124 ± 50	0.31
Serum sodium (mmol/L)	139 ± 4	139 ± 4	139 ± 5	0.24
Haemoglobin (mmol/L)	8.3 ± 1.2	8.4 ± 1.2	8.3 ± 1.2	0.49
Aetiology (%)				
Ischaemic	43%	45%	40%	0.24
Non-ischaemic	57%	55%	60%	
Atrial fibrillation	42%	42%	43%	0.89
Medication at admission				
Diuretics	62%	62%	62%	0.89
ACE-inhibitors/ARB	56%	55%	56%	0.85
Beta blockers	42%	41%	43%	0.58
Digoxin	19%	17%	21%	0.18
Spironolactone	16%	15%	17%	0.50
Comorbidities				
Hypertension	35%	33%	39%	0.14
COPD	25%	22%	29%	0.06
Diabetes mellitus II	20%	20%	19%	0.79
Peripheral vascular disease	16%	16%	18%	0.60
Renal dysfunction	8%	8%	8%	0.95
Cerebrovascular accident	8%	8%	8%	0.95
Arthritis	7%	5%	9%	0.14
Mean number of comorbidities	1.1 ± 1.0	1.0 ± 1.0	1.2 ± 1.1	0.16
No comorbidities	34%	36%	31%	
1–2 comorbidities	56%	54%	59%	
2–6 comorbidities	10%	10%	10%	
Duration of heart failure (y)	2.5 ± 4.8	2.8 ± 5.6	2.0 ± 3.3	0.19
Heart failure symptoms				
Mean number of HF symptoms	4.0 ± 1.3	3.9 ± 1.3	4.6 ± 1.4	0.0001*
No symptoms	2%	0.3%	0.4%	
1–2 symptoms	10%	14%	5.4%	
3–4 symptoms	41%	48%	30%	
5–6 symptoms	47%	37%	66%	
Dyspnoea	95%	93%	97%	0.017
Fatigue	87%	82%	95%	0.0001*
Coughing	70%	68%	73%	0.17
Oedema	64%	62%	67%	0.20
Sleep disturbance	62%	51%	79%	0.0001*
Loss of appetite	51%	40%	68%	0.0001*
Depression				
Mean CES-D total score (range: 0–60)	15.6 ± 11	8 ± 4.5	26 ± 8.3	0.0001*
Symptoms of depression (CES-D ≥ 16)	41%			

patients were asked whether they had experienced the following symptoms during the last month: ankle oedema during the day, ankle oedema when getting out of bed in the morning, sleep disturbance, fatigue, breathlessness at rest and during exertion, orthopnoea, coughing, dry cough or loss of appetite. These ten symptoms were clustered in six symptom indexes: oedema, sleep disturbance, fatigue, dyspnoea, coughing and loss of appetite. A total HF symptom score was obtained from the sum of the six symptom indexes.

2.3. Statistical analyses

Descriptive statistics were used to characterize the study population. Means, medians and standard deviations are presented for depressive symptoms, demographic and clinical data and HF symptoms (Table 1).

Student's *t*-tests and Mann Whitney tests for continuous variables and chi square tests for categorical variables were performed to compare demographic and clinical characteristics and HF symptoms between patients with or without depressive symptoms. A multivariable logistic regression analysis was utilized to define the independent association between depressive symptoms and demographic and clinical characteristics and HF symptoms. The multivariate model was built by entering those variables that had a univariate p value <0.15 (e.g. sex, LVEF, hypertension, COPD, arthritis, number of HF symptoms, dyspnoea, fatigue, sleep disturbance and loss of appetite) and retaining those variables with $p<0.05$ in the final model.

3. Results

3.1. Participants

Between November 2002 and April 2004, 737 patients who met the criteria for the COACH study, agreed to participate and gave informed consent. Six hundred and eighty one of these patients filled out the CES-D questionnaire; however, 109 of these patients did not complete the structured interview about the ten HF symptoms. Therefore, 572 HF patients were included in this sub-study. There were no significant differences in basic demographics (age, sex) and clinical variables (LVEF, NYHA class) between patients with or without complete data sets.

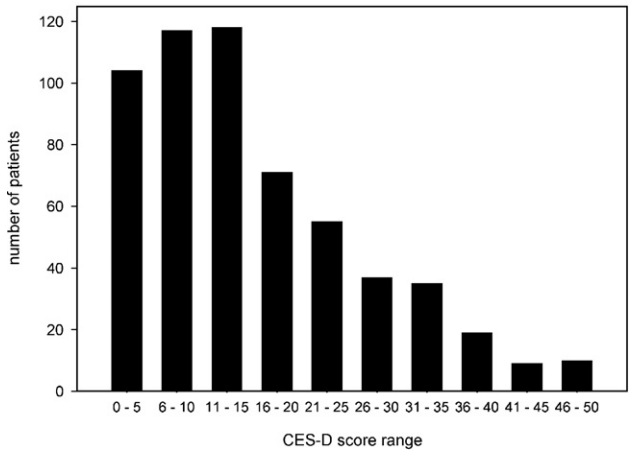

Fig. 1. CES-D total score in population ($n=572$).

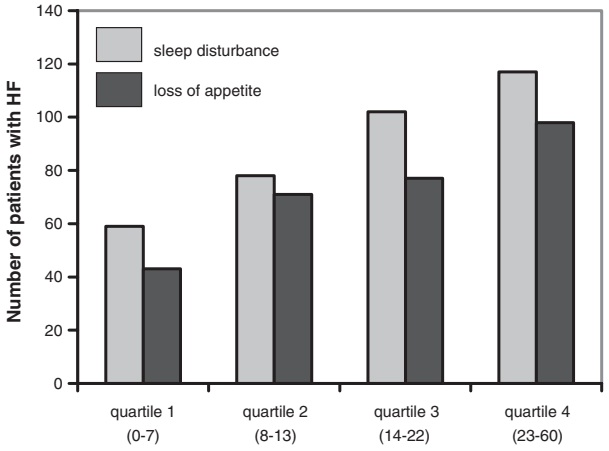

Fig. 2. Number of patients ($n=572$) with sleep disturbance and loss of appetite among the 4 quartiles of the CES-D score.

On average, patients were 71±12 years of age and most patients (62%) were male (Table 1). The majority of patients had a low educational level, were living with a partner and had suffered from HF for more than two and a half years. On admission, most patients were in NYHA functional class III (51%) and IV (43%). The mean LVEF was 34%±15. On average, patients had one medical comorbidity (range 0–6). One third of patients were hypertensive (35%), Chronic Obstructive Pulmonary Disease was present in 25% of the patients and type II diabetes mellitus in 20%. All patients were on standard medical treatment regimens with ACE-inhibitors, beta blockers and diuretics.

3.2. HF symptoms

Patients reported on average four symptoms of HF; less than two percent of the patients reported no symptoms, 30% had five symptoms and 17% had six symptoms of HF at the time of measurement. The most frequently reported symptoms of HF were dyspnoea (95%) and fatigue (87%). More than two thirds of the patients had cough, oedema and sleep disturbance. Fifty one percent of patients had loss of appetite (Table 1).

3.3. Prevalence of depressive symptoms

The mean total score on the CES-D in this study population was 15.6±11 (0–60) (Fig. 1). More than 41% of the patients had depressive symptoms (score CES-

D ≥ 16) (Table 1). Importantly, on all 20 items of the CES-D significant differences were found between patients with and without depressive symptoms, including the somatic items like loss of appetite and sleep disturbance.

Loss of appetite and sleep disturbance are two common somatic symptoms in HF patients as well as in patients with depression. Of the non-depressed HF patients 40% reported loss of appetite and 51% have sleeping difficulties. But patients with depressive symptoms more often report loss of appetite (68%) and sleeping difficulties (79%) (Table 1). Although sleep disturbance and loss of appetite are both symptoms of HF and symptoms of depression, patients with depressive symptoms score significantly worse on these two items (Fig. 2). When these two items were removed from the CES-D, 36% of the HF patients still reported depressive symptoms (CES-D ≥ 16).

3.4. Differences in demographic and clinical characteristics between patients with and without depressive symptoms

Based on the CES-D score we compared patients without (score <16) or with (score ≥16) depressive symptoms. Univariate analyses among patients with or without depressive symptoms indicated that more women than men suffered from depressive symptoms: 48% versus 36% ($\chi^2 = 8.1$, $p < 0.05$) (Table 1). No significant differences were found between patients with and without depressive symptoms according to age, living with a partner and educational level.

With respect to clinical characteristics, like LVEF, NYHA functional class at admission, aetiology, duration of HF and the number and nature of medical co-morbidities, no significant differences were seen between the two groups (Table 1).

3.5. Relation between depressive symptoms and HF symptoms

Compared to patients without depressive symptoms, patients with depressive symptoms had more symptoms of HF ($z = -7.1$ $p < 0.01$). Also the nature of these symptoms was different between the two groups. Patients with depressive symptoms more often reported dyspnoea ($p < 0.01$), fatigue, sleep disturbance and loss of appetite ($p < 0.01$). In a multivariable logistic regression analysis female sex, COPD, sleep disturbances and loss of appetite were all independently associated with depressive symptoms (Table 2).

Table 2
Summary statistics for multivariable logistic regression model of depressive symptoms and demographic and clinical variables

Variable	Odds ratio	95% CI	*P* value
Female sex	1.68	1.14–2.48	0.009
COPD	2.11	1.35–3.30	0.001
Sleep disturbance	3.45	2.03–5.85	0.001
Loss of appetite	2.28	1.58–4.33	0.001

CI = confidence interval, COPD = chronic obstructive pulmonary disease.

4. Discussion

4.1. Depressive symptoms

In this study we found a very high prevalence of depressive symptoms among a group of hospitalised, elderly HF patients. This is consistent with findings in several other studies. Recent studies have shown that depression is common in HF patients with prevalence rates in outpatients ranging from 11% to 25% [5,9,13,15,22]. In our study of hospitalised elderly patients we found that 41% of patients with HF reported depressive symptoms. This is comparable to some other smaller studies that found rates of 14–77% [4,5,8,13,15,17,22,23]. One reason for the wide range of prevalence rates reported across studies is the use of different definitions [23]. If depression is defined as a clinical diagnosis, listed in the patient record as an active problem, the prevalence will be low. Faris [15] reports that this is an underestimation of the prevalence of depressive symptoms. Sometimes the term depression is defined as 'major depression' as defined by DSM-IV, if this is the case, lower incidence rates for depression are also found (9–26%) [23]. If depression is defined as mild or moderate or as having depressive symptoms then the incidence is much higher. In our study, we defined depression as having depressive symptoms.

It has also been reported in other studies, that patients with HF suffer more frequently from moderate to severe depression than patients with other chronic diseases (e.g. type II diabetes, cancer). In a study of 203 older patients with type II diabetes (mean age: 67 years) only 10% were depressed [24]. A Dutch study of 475 patients with cancer (mean age: 58.6 years), 19.7% had a CES-D score ≥ 16 [7,25] and in a community based sample of elderly people in the Netherlands, 15% were found to be depressed [3]. The high rate of depressive symptoms in HF patients may be due to the worse functional status [26,27], decrease in quality of life [28,29] the high level of psychological distress [30,31] and biological abnormalities [10,32].

In our study female sex, COPD, sleep disturbances and loss of appetite were associated with depressive symptoms. Gottlieb et al. [9] also reported that women are more likely to experience depression. In their study among 155 outpatient HF patients 64% of the women are depressed compared to only 44% of the men. It is also known that in physically healthy subjects, women are twice as likely to be diagnosed with depressive symptoms than men [7,25,33]. None of the other demographic and clinical parameters were associated with depressive symptoms in this study population.

COPD is a common comorbidity in HF patients and in our study an independent risk factor associated with

depressive symptoms. Symptoms like dyspnoea and fatigue experienced by HF patients with COPD do interact with each other and can lead to increased frequency and severity of symptoms of HF, which in turn can lead to symptoms of depression.

There seems to be a considerable overlap between depressive symptoms and symptoms of HF. For example fatigue, low mood, lost of interest in usual activities and sleeplessness are common in both [15,18,34]. In our study, we found that sleep disturbances and loss of appetite were both independently associated with depressive symptoms. The connection between these symptoms of depression in HF patients may lie in shared mechanisms in HF and depression. Both in HF patients and depressive patients activation of the sympathetic nervous system, elevated levels of cytokines, a decreased heart rate variability (HRV) and rhythm disturbances have been described [10,32,35–37]. For example in both patients with HF and patients with depression a higher level of tumor necrosis factor alpha (TNF-α) has been found [35,36], which is linked to cardiac cachexia [35,36]. Sleep disturbance is a symptom also often seen in both depressive and HF patients. The shared factor in this can be the low HRV in both groups of patients [10,18,23]. Despite the overlap in symptoms, we found a significant difference in the amount and nature of HF symptoms between patients with and without depressive symptoms. In further analyses only two somatic items of the CES-D had an overlap with the questions about HF symptoms in the structured interview. If these two somatic items (sleep disturbance and loss of appetite) were removed from the CES-D, a lot of HF patients (36%) still reported depressive symptoms (CES-D $\geq$ 16). Furthermore for these two items, patients with depressive symptoms score significantly worse on both the CES-D and the structured interview.

In conclusion: In the present study we assessed the occurrence of depressive symptoms in elderly HF patients and studied the relation with demographic and clinical characteristics and HF symptoms. Depressive symptoms are very prominent in hospitalised, elderly HF patients, especially in women and in those with more pronounced symptomatology. Several studies have suggested that depression and depressive symptoms in HF patients are linked to adverse outcomes. Therefore, treatment of depression or depressive symptoms, especially if they continue after discharge, is important as these symptoms may hamper successful treatment of HF and have an adverse impact on the lives of elderly, hospitalised HF patients.

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